Pharmacy Medical Necessity Guidelines: Non-Insulin Antidiabetic Agents

Effective: January 1, 2021

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	RX	Department to Review	RXUM

These pharmacy medical necessity guidelines apply to the following:

Commercial Products

☐ Tufts Health Plan Commercial products – large group plans
☐ Tufts Health Plan Commercial products – small group and individual plans
☐ Tufts Health Freedom Plan products – large group plans
☐ Tufts Health Freedom Plan products – small group plans
- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

Tufts Health Public Plans Products

☐ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product)
☒ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans
☐ Tufts Health RITogether – A Rhode Island Medicaid Plan

Fax Numbers:
RXUM: 617.673.0988

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

Biguanides

Metformin is indicated for the management of type 2 diabetes mellitus when hyperglycemia cannot be managed with diet and exercise alone.

Coverage of Biguanides

Medication Name	Coverage	Quantity Limit
Preferred DPP-4 Inhibitors		
Metformin 500, 850, 1000 mg tablets (generic Glucophage)	Covered	N/A
Metformin ER 500, 750 mg tablet (generic Glucophage XR)	Covered	N/A
Riomet 500 mg/mL (metformin) solution	**< 13 years old:** Covered; Brand Preferred **≥ 13 years old:** PA; Brand Preferred	N/A
Non-Preferred DPP-4 Inhibitor		
Metformin ER 500, 1000 mg tablet (generic Glumetza)	PA	N/A
Metformin ER 500, 1000 mg tablet (generic Fortamet)	PA	N/A
Riomet ER 500 mg/mL suspension (metformin ER)	PA	N/A

ER = Extended-Release; PA = Prior Authorization

Dipeptidyl Peptidase-4 (DPP-4) Inhibitors:

The DPP-4 inhibitors are approved as adjuncts to diet and exercise to control glycemic control in adults with type 2 diabetes.

Coverage of DPP-4 Inhibitors

Medication Name	Coverage	Quantity Limit
Preferred DPP-4 Inhibitors		
Januvia (sitagliptin)	Covered	N/A
Onglyza (saxagliptin)	Covered	N/A
Tradjenta (linagliptin)	Covered	N/A
Non-Preferred DPP-4 Inhibitor		
Alogliptin	PA;QL	1 tablet per day

PA = Prior Authorization; QL = Quantity Limit

Sodium Glucose Cotransporter-2 (SGLT-2) Inhibitors:
All of the SGLT-2 inhibitors are approved as an adjunct to diet and exercise to improve glycemic control in adults. Additional indications are as follows:

- **Farxiga (dapagliflozin):**
  - Reduce risk of hospitalization for heart failure in adults with type 2 diabetes and established (CVD) or multiple CV risk factors
  - Reduce risk of CV death and hospitalization for heart failure in adults with heart failure (NYHA II-IV) with reduced ejection fraction
- **Jardiance (empagliflozin):**
  - Reduce risk of CV death in adult patients with type 2 diabetes and established CVD
- **Invokana (canagliflozin):**
  - Reduce risk of major CV events (CV death, myocardial infarction, nonfatal stroke) in adults with type 2 diabetes and established CVD
  - Reduce risk of end-state kidney disease, doubling of serum creatinine, CV death, and hospitalization for heart failure in adults with type 2 diabetes and diabetic nephropathy with albuminuria greater than 300 mg/day

Coverage of SGLT-2 Inhibitors

Medication Name	Coverage	Quantity Limit
Preferred SGLT-2 Inhibitors		
Farxiga (dapagliflozin)	Covered;QL	1 tablet per day
Invokana (canagliflozin)	Covered;QL	**100 mg:** 2 tablets per day **300 mg:** 1 tablet per day
Jardiance (empagliflozin)	Covered;QL	1 tablet per day
Non-Preferred SGLT-2 Inhibitor		
Steglatro (ertugliflozin)	PA;QL	1 tablet per day

PA = Prior Authorization; QL = Quantity Limit

Combination Products

Coverage of Combination Products

Medication Name	Coverage	Quantity Limit
DPP-4/Metformin Combination Products		
Preferred DPP-4 Inhibitor/Metformin Combination Products		
Janumet (sitagliptin/metformin)	Covered;QL	2 tablets per day
Janumet XR (sitagliptin/metformin ER)	Covered;QL	**50/500 mg, 50/1000 mg:** 2 tablets per day **100/1000 mg:** 1 tablet per day
Jentadueto (linagliptin/metformin)	Covered;QL	2 tablets per day
Jentadueto XR (linagliptin/metformin ER)	Covered;QL	**5/1000 mg:** 1 tablet per day **2.5/1000 mg:** 2 tablets per day
Kombiglyze XR (saxagliptin/metformin ER)	Covered;QL	**5/500 mg, 5/1000 mg:** 1 tablet per day **2.5/1000 mg:** 2 tablets per day
Non-Preferred DPP-4 Inhibitor/Metformin Combination Product		
Alogliptin/metformin	PA;QL	2 tablets per day
DPP-4/Thiazolidinedione Combination Product		
Alogliptin/Pioglitazone	PA;QL	1 tablet per day
SGLT-2/Metformin Combination Products		
Preferred SGLT-2/Metformin Combination Products		
Invokamet (canagliflozin/metformin)	Covered;QL	2 tablets per day
Invokamet XR (canagliflozin/metformin ER)	Covered;QL	2 tablets per day

Synjardy (empagliflozin/metformin)	Covered;QL	2 tablets per day
Synjardy XR (empagliflozin/metformin ER)	Covered;QL	**10/1000 mg, 25/1000 mg:** 1 tablet per day **12.5/1000 mg, 5/1000 mg:** 2 tablets per day
Xigduo XR (dapagliflozin/metformin ER)	Covered;QL	**10/1000 mg, 10/500 mg:** 1 tablet per day **2.5/1000 mg, 5/1000 mg, 5/500 mg:** 2 tablets per day
Non-Preferred SGLT-2/Metformin Combination Product		
Segluromet (ertugliflozin)	PA;QL	2 tablets per day
DPP-4 Inhibitor/SGLT-2 Inhibitor Combination Product		
Glyxambi (empagliflozin/linagliptin)	PA;QL	1 tablet per day

PA = Prior Authorization; QL = Quantity Limit

Glucagon-like Peptide-1 (GLP-1) Agonists:

GLP-1 agonists are approved as adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes. The following agents have additional indications:

- **Ozempic (semaglutide):**
  - Reduce risk of major adverse CV events in adults with T2DM and established CVD
- **Trulicity (dulaglutide):**
  - Reduce risk of major adverse CV events in adults with T2DM who have established CVD or multiple CV risk factors
- **Victoza (liraglutide):**
  - Adjunct to diet and exercise to improve glycemic control in patients 10 years of age and older with T2DM
  - Reduce risk of major adverse CV events in adults with T2DM and established CVD

GLP-1 agonists have varying administration frequencies (e.g, daily, weekly), which should be taken into consideration when choosing the most appropriate treatment option for a patient.

Coverage of GLP-1 Receptor Agonists

Medication Name	Administration Frequency	Coverage	Quantity Limit
Preferred GLP-1 Agonists			
Bydureon (exenatide extended-release) injection	Once weekly	Covered;QL	4 pens per 28 days
Byetta (exenatide) injection	Twice daily	Covered;QL; Brand Preferred	1 pen per 30 days
Trulicity (dulaglutide) injection	Once weekly	Covered;QL; Preferred Drug	4 pens per 28 days
Victoza (liraglutide) injection	Once daily	Covered;QL	3 pens per 28 days
Non-Preferred GLP-1 Agonists and Combination Products			
Bydureon BCise (exenatide extended-release) injection	Once weekly	PA;QL	4 autoinjectors per 28 days
Ozempic (semaglutide) injection	Once weekly	PA;QL	**0.25 or 0.5 mg/dose pen:** 1 pen per 28 days **1 mg/dose pen:** 2 pens per 28 days
Rybelsus (semaglutide) tablet	Once daily	PA;QL	1 tablet per day
Soliqua (insulin glargine/ lixisenatide) injection	Once daily	PA;QL	6 pens per 30 days
Xultophy (insulin degludec/liraglutide) injection	Once daily	PA;QL	5 pens per 30 days

COVERAGE GUIDELINES

The plan may authorize coverage of a non-insulin antidiabetic medication for members when the criteria are met and limitations do not apply:

INITIAL APPROVAL

Biguanides

Metformin extended-release tablet (generic Fortamet, generic Glumetza)

1. The Member has a diagnosis of type 2 diabetes

AND

2. Medical records documenting an inadequate response or adverse reaction despite 90 days of therapy with a generic metformin ER formulation at the requested dose that is AB-rated to Glucophage XR have been provided

AND

3. **Generic Glumetza requests only:** Provider has submitted a clinical rationale for the use of generic Glumetza instead of other available metformin formulations

Riomet (metformin solution) for members 13 years of age and older, Riomet ER (metformin extended-release solution)

1. The Member has a diagnosis of type 2 diabetes

AND

2. The Member has ONE of the following:
   a. Medical necessity for a liquid formulation (inability to swallow oral medications)

OR

   b. Medical records documenting an inadequate response despite 90 days of therapy with the metformin tablet formulation, or an allergic reaction or adverse reaction to the metformin tablet formulation that is not class specific (i.e., nausea, diarrhea)

AND

3. **Riomet ER only:** Medical records documenting an inadequate response despite 90 days of therapy with the immediate release metformin solution formulation have been submitted

Dipeptidyl Peptidase-4 (DPP-4) Inhibitors

Alogliptin:

1. The Member has a diagnosis of type 2 diabetes

AND

2. The Member has **ONE** of the following:
   a) An inadequate response (defined as at least 90 days of therapy within a 120-day time period) to metformin used in combination with ONE of the following DPP-4 inhibitors:
      - Januvia (sitagliptin)
      - Onglyza (saxagliptin)
      - Tradjenta (linagliptin)

OR

   b) **BOTH** of the following:
      - Adverse reaction or contraindication to metformin

AND

      - Inadequate response (defined as at least 90 days of therapy within a 120-day time period) to **ONE** of the following:
        (1) Januvia (sitagliptin)

(2) Onglyza (saxagliptin)
(3) Tradjenta (linagliptin)

OR

c) **BOTH** of the following:
- Inadequate response (defined as at least 90 days of therapy within a 120-day time period), adverse reaction, or contraindication to metformin

AND

- Adverse reaction to **ONE** of the following:
(1) Januvia (sitagliptin)
(2) Onglyza (saxagliptin)
(3) Tradjenta (linagliptin)

OR

d) **BOTH** of the following:
- Inadequate response (defined as at least 90 days of therapy within a 120-day time period), adverse reaction or contraindication to metformin

AND

- Contraindication to **ALL** of the following:
(1) Januvia (sitagliptin)
(2) Onglyza (saxagliptin)
(3) Tradjenta (linagliptin)

<u>Sodium Glucose Co-Transporter-2 (SGLT-2) Inhibitors</u>

Steglatro (ertugliflozin):

1. The Member has a diagnosis of type 2 diabetes

AND

2. The Member has ONE of the following:
a) An inadequate response (defined as at least 90 days of therapy within a 120-day time period) to metformin used in combination ONE of the following:
- Farxiga (dapagliflozin)
- Invokana (canagliflozin)
- Jardiance (empagliflozin)

OR

b) BOTH of the following:
- Adverse reaction or contraindication to metformin

AND

- Inadequate response (defined as at least 90 days of therapy within a 120-day time period) to ONE of the following:
(1) Farxiga (dapagliflozin)
(2) Invokana (canagliflozin)
(3) Jardiance (empagliflozin)

OR

c) **BOTH** of the following:
- Inadequate response (defined as at least 90 days of therapy within a 120-day time period), adverse reaction, or contraindication to metformin

AND

- Adverse reaction to **ONE** of the following:
(1) Farxiga (dapagliflozin)
(2) Invokana (canagliflozin)

(3) Jardiance (empagliflozin)

OR

d) **BOTH** of the following:
- Inadequate response (defined as at least 90 days of therapy within a 120-day time period), adverse reaction or contraindication to metformin

AND

- Contraindication to ALL of the following:
  (1) Farxiga (dapagliflozin)
  (2) Invokana (canagliflozin)
  (3) Jardiance (empagliflozin)

SGLT-2 and DPP-4 Combination Products

Alogliptin/metformin, alogliptin/pioglitazone, Glyxambi (emagliflozin/linagliptin), Segluromet (ertugliflozin/metformin)

1. The Member has a diagnosis of type 2 diabetes

AND

2. The Member has **ONE** of the following:
   a) An inadequate response (defined as at least 90 days of therapy within a 120-day time period) to metformin used in combination with at least one of the non-metformin agents in the requested combination

OR

   b) **BOTH** of the following:
   - Adverse reaction or contraindication to metformin

AND

   - Inadequate response (defined as at least 90 days of therapy within a 120-day time period) to at least one of the non-metformin agents in the requested combination

OR

   c) **BOTH** of the following:
   - Inadequate response (defined as at least 90 days of therapy within a 120-day time period), adverse reaction, or contraindication to metformin

AND

   - Adverse reaction to at least one of the non-metformin agents in the requested combination

Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

Bydureon BCise (exenatide extended-release), Ozempic (semaglutide), Rybelsus (semaglutide), Soliqua (insulin glargine/lixisenatide), Xultophy (insulin degludec/liraglutide):

1. The Member has a diagnosis of type 2 diabetes

AND

2. The Member has **ONE** of the following:
   a) An inadequate response (defined as at least 90 days of therapy within a 120-day time period) to metformin used in combination **ONE** of the following GLP-1 agonists:
   - Bydureon (exenatide extended-release pen)
   - Byetta (exenatide)
   - Trulicity (dulaglutide)
   - Victoza (liraglutide)

OR

   b) **BOTH** of the following:

- Adverse reaction or contraindication to metformin

AND

- Inadequate response (defined as at least 90 days of therapy within a 120-day time period) to **ONE** of the following:
  (1) Bydureon (exenatide extended-release pen)
  (2) Byetta (exenatide)
  (3) Trulicity (dulaglutide)
  (4) Victoza (liraglutide)

OR

c) **BOTH** of the following:
- Inadequate response (defined as at least 90 days of therapy within a 120-day time period), adverse reaction, or contraindication to metformin

AND

- Adverse reaction to ONE of the following:
  (1) Bydureon (exenatide extended-release pen)
  (2) Byetta (exenatide)
  (3) Trulicity (dulaglutide)
  (4) Victoza (liraglutide)

OR

d) **BOTH** of the following:
- Inadequate response (defined as at least 90 days of therapy within a 120-day time period), adverse reaction or contraindication to metformin

AND

- Contraindication to **ALL** of the following:
  (1) Bydureon (exenatide extended-release pen)
  (2) Byetta (exenatide)
  (3) Trulicity (dulaglutide)
  (4) Victoza (liraglutide)

LIMITATIONS

1. Requests for brand-name products, which have AB-rated generics, will be reviewed according to non-covered medications criteria. In those instances in which the brand name agent is preferred over the generic, requests for the generic will be reviewed according to the Brand Name criteria from the perspective that the brand is preferred over the generic.
2. Requests for quantities that exceed the quantity limit will be reviewed according to the drugs with Quantity Limitations criteria.
3. Quantity limitations are as follows:

Medication Name	Quantity Limit
Alogliptin	1 tablet per day
Alogliptin/metformin	2 tablets per day
Alogliptin/pioglitazone	1 tablet per day
Bydureon (exenatide extended-release) injection	4 pens per 28 days
Byetta (exenatide) injection	1 pen per 30 days
Bydureon BCise (exenatide extended-release) injection	4 autoinjectors per 30 days
Farxiga (dapagliflozin)	1 tablet per day
Glyxambi (empagliflozin/linagliptin)	1 tablet per day
Invokamet (canagliflozin/metformin)	2 tablets per day
Invokamet XR (canagliflozin/metformin ER)	2 tablets per day
Invokana (canagliflozin)	**100 mg:** 2 tablets per day **300 mg:** 1 tablet per day
Jardiance (empagliflozin)	1 tablet per day
Janumet (sitagliptin/metformin)	2 tablets per day

Medication Name	Quantity Limit
Janumet XR (sitagliptin/metformin ER)	**50/500 mg, 50/1000 mg:** 2 tablets per day **100/1000 mg:** 1 tablet per day
Jentadueto (linagliptin/metformin)	2 tablets per day
Jentadueto XR (linagliptin/metformin ER)	**5/1000 mg:** 1 tablet per day **2.5/1000 mg:** 2 tablets per day
Kombiglyze XR (saxagliptin/metformin ER)	**5/500 mg, 5/1000 mg:** 1 tablet per day **2.5/1000 mg:** 2 tablets per day
Ozempic (semaglutide) injection	**0.25 or 0.5 mg/dose pen:** 1 pen per 28 days **1 mg/dose pen:** 2 pens per 28 days
Rybelsus (semaglutide) tablet	1 tablet per day
Segluromet (ertugliflozin)	2 tablets per day
Soliqua (insulin glargine/ lixisenatide) injection	6 pens per 30 days
Steglatro (ertugliflozin)	1 tablet per day
Synjardy (empagliflozin/metformin)	**10/1000 mg, 25/1000 mg:** 1 tablet per day **12.5/1000 mg, 5/1000 mg:** 2 tablets per day
Synjardy XR (empagliflozin/metformin ER)	**10/1000 mg, 25/1000 mg:** 1 tablet per day **12.5/1000 mg, 5/1000 mg:** 2 tablets per day
Trulicity (dulaglutide) injection	4 pens per 28 days
Xigduo XR (dapagliflozin/metformin ER)	**10/1000 mg, 10/500 mg:** 1 tablet per day **2.5/1000 mg, 5/1000 mg, 5/500 mg:** 2 tablets per day
Xultophy (insulin degludec/liraglutide) injection	5 pens per 30 days
Victoza (liraglutide) injection	3 pens per 28 days

CODES

None

REFERENCES

1. American Diabetes Association. Standards of Medical Care in Diabetes – 2020. *Diabetes Care*. 2020 Jan;43(Supplement 1);S1-S212.
2. Bydureon (exenatide extended-release) [prescribing information]. February 2020.
3. Bydureon BCise (exenatide extended-release) [prescribing information]. AstraZeneca Pharmaceuticals: Wilmington, DE; February 2020.
4. Byetta (exenatide) [prescribing information]. AstraZeneca Pharmaceuticals: Wilmington, DE; February 2020.
5. Farxiga (dapagliflozin) [prescribing information]. AstraZeneca Pharmaceuticals: Wilmington, DE; May 2020.
6. Fortamet (metformin extended-release) [prescribing information]. Shinogi Pharmaceuticals: Florham Park, NJ; November 2018.
7. Glucophage/Glucophage XR (metformin/metformin extended-release) [prescribing information]. Bristol-Myers Squibb: Princeton, NJ; December 2019.
8. Glumetza (metformin extended-release) [prescribing information]. Salix Pharmaceuticals: Bridgewater, NJ; August 2019.
9. Invokamet (canagliflozin/metformin) [prescribing information]. Janssen Pharmaceuticals, Inc: Titusville, NJ; August 2020.
10. Invokamet XR (canagliflozin/metformin extended-release) [prescribing information]. Janssen Pharmaceuticals, Inc: Titusville, NJ; August 2020.
11. Invokana (canagliflozin) [prescribing information]. Janssen Pharmaceuticals, Inc: Titusville, NJ; August 2020.
12. Janumet (sitagliptin/metformin) [prescribing information]. Merck and Co: Whitehouse Station, NJ: August 2019.
13. Janumet XR (sitagliptin/metformin extended-release) [prescribing information]. Merck and Co: Whitehouse Station, NJ; August 2019.

14. Januvia (sitagliptin) [prescribing information]. Merck and Co: Whitehouse Station, NJ; August 2019.
15. Jardiance (empagliflozin) [prescribing information]. Boehringer Ingelheim Pharmaceuticals, Inc: Ridgefield, CT; January 2020.
16. Jentadueto (linagliptin/metformin) [prescribing information]. Boehringer Ingelheim: Ridgefield, CT; March 2020.
17. Jentadueto XR (linagliptin/metformin extended-release) [prescribing information]. Boehringer Ingelheim: Ridgefield, CT; March 2020.
18. Kazano (alogliptin/metformin) [prescribing information]. Takeda Pharmaceuticals: Deerfield, IL; June 2019.
19. Kombiglyze XR (saxagliptin/metformin extended-release) [prescribing information]. AstraZenec Pharmaceuticals: Wilmington, DE; October 2019.
20. Nesina (alogliptin) [prescribing information]. Takeda Pharmaceuticals: Deerfield, IL; June 2019.
21. Onglyza (saxagliptin) [prescribing information]. AstraZeneca Pharmaceuticals: Wilmington, DE; October 2019.
22. Oseni (alogliptin/pioglitazone) [prescribing information]. Takeda Pharmaceuticals: Deerfield, IL; June 2019.
23. Ozempic (semaglutide) [prescribing information]. Novo Nordisk: Plainsboro, NJ; September 2020.
24. Riomet (metformin) [prescribing information]. Sun Pharmaceutical Industries: Cranbury, NJ; Decemberber 2018.
25. Riomet ER (metformin extended-release) [prescribing information]. August 2019. Sun Pharmaceutical Industries: Cranbury, NJ; November 2019.
26. Rybelsus (semaglutide) [prescribing information]. Novo Nordisk: Plainsboro, NJ; January 2020.
27. Soliqua (insulin glargine/lixisenatide) [prescribing information]. Sanofi-Aventis: Bridgewater, NJ; November 2019.
28. Steglatro (ertugliflozin) [prescribing information]. Merck and Co: Whitehouse Station, NJ; January 2020.
29. Synjardy (empagliflozin/metformin) [prescribing information]. Boehringer Ingelheim Pharmaceuticals, Inc: Ridgefield, CT; January 2020.
30. Synjardy XR (empagliflozin/metformin extended-release) [prescribing information]. Boehringer Ingelheim Pharmaceuticals, Inc: Ridgefield, CT; January 2020.
31. Tradjenta (linagliptin) [prescribing information]. Boehringer Ingelheim Pharmaceuticals, Inc: Ridgefield, CT; March 2020.
32. Trulicity (dulaglutide) [prescribing information]. Eli Lilly: Indianapolis, IN; September 2020.
33. Victoza (liraglutide) [prescribing information]. Novo Nordisk: Plainsboro, NJ; August 2020.
34. Xigduo XR (dapagliflozin/metformin extended-release) [prescribing information]. AstraZeneca Pharmaceuticals: Wilmington, DE; January 2020.
35. Xultophy (insulin degludec/liraglutide) [prescribing information]. Novo Nordisk: Plainsboro, NJ; November 2019.

APPROVAL HISTORY

November 24, 2020: Reviewed by Pharmacy & Therapeutics Committee.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of

benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.